REMARKS

REJECTIONS UNDER 35 USC §112

The examiner has rejected claims 55-99 under the first paragraph of 35 USC §112 for lack of adequate written description. Applicants have amended these claims to recite DNA constructs containing the promoter of the *B. vulgaris* V-ATPase subunit c in isoform 2 together with a heterologous gene. Applicants maintain that gene orthologs have strong sequence homology and should possess the same function and expression patterns, and make the amendment solely to further the present prosecution.

The examiner has rejected claims 55 and 62 under the second paragraph of §112 for lack of definiteness in use of the term "functional equivalent." Applicants introduce new claim 100 herein, which is drawn to DNA constructs containing functional equivalents of the *B. vulgaris* promoter at issue, together with heterologous genes. Claims 55 and 62 no longer recite this language. In creating this new independent claim, applicants submit that the referant of "functional equivalent" is now clear, and further submit that the definition of this term is also clear to one of ordinary skill in the art.

The examiner further rejects claims 55, 61, and 74 as indefinite in their use of the word "gene," stating that "the definition of gene given by one possessing the ordinary level of skill in the art would not exclude promoter sequences, noncoding

sequences and termination sequences" (advisory action, p.4). Applicants append hereto an excerpt from the Oxford Dictionary of Biotechnology which shows the entry for "gene" in that dictionary. In classical genetics, "gene" referred to a particular phenotypic characteristic, and was defined in terms of mutation or recombination rates. Under the central dogma of protein synthesis, "the 'one gene-one enzyme' hypothesis, ... a gene consisted of DNA that coded for a protein that performed the functions associated with the phenotypic expression of the gene." That definition has been modified in current molecular genetics in part to reflect the presence of regulatory sequences *associated with* genomic DNA.

As this entry demonstrates, genes are stretches of DNA that code for proteins. The genes may *contain* regulatory sequences, and the coded-for proteins themselves may serve regulatory functions with regard to other genes, yet the term "gene" is necessarily correlated with an associated protein. "Promoter sequences, noncoding sequences and termination sequences" are simply not genes (advisory action, p.4). Applicants submit that the definition of the word "gene" is sufficiently definite to one of skill in the art.

The examiner rejects claim 59 as indefinite, stating that "the manner in which the first and second promoters are regulated cannot be discerned from the claim" (*id.*). Claim 59 depends from claim 55, which recites a DNA construct comprising the specified promoter and a heterologous gene. The specification indicates that the claimed promoters are regulated at least in part by subjection to biotic or abiotic stress.

In contrast, the commonly-used 35s CaMV promoter, for example, does not respond to these stresses, but its routine use indicates that one of skill in the art could readily ascertain to what it *does* respond (*see*, *e.g.*, p.12:31-33, and p.13:1-13). Some promoters may respond both to biotic and abiotic stresses in the manner of the presently claimed promoters, and additionally respond to other triggers.

The language of claim 59 is therefore straightforward and definite. The claimed DNA construct comprises the specified V-ATPase promoter, regulated by biotic or abiotic stress, the heterologous gene, and a second promoter "which can be regulated in a different manner." Applicants submit that this is sufficiently definite for one of ordinary skill in the art.

The examiner further rejects claim 61 as indefinite. Applicants respectfully direct the examiner's attention to page 6 of the specification, where suitable resistance-mediating genes and other genes of interest are exemplified. Within the present art, the scope of coverage would be readily apparent to one of skill therein, given the disclosure set forward in the specification. Applicants are uncertain how selection markers and resistance mediating genes are to be categorized if not as genes of medicinal, agronomical or other interest.

Claims 74 and 78 have been amended for clarity.

Claims 96 and 97 have also been amended for clarity.

The examiner rejects claims 90 and 91 as being incomplete. Applicants append hereto a second entry from the Oxford Dictionary of Biotechnology, showing the

definition of gene expression. The entry reads as follows.

> gene expression - the process by which the information carried by a gene or genes becomes manifest as the phenotype. It involves *transcription* of the gene into complementary RNA sequences and, for structural genes, subsequent *translation* of mRNA into polypeptide chains and their assembly into the ultimate protein products.

(p.258.) According to this commonly accepted definition of "gene expression," applicants respectfully submit that one of skill in the art would understand both transcription and translation to take place in the process of the claims at issue.

The examiner rejects claims 92-95 for omitting the step of expression, asserting that transformation of a plant with a construct would not necessarily result in expression of the construct in the transformed plant. Applicants recognize that as a general rule, the examiner is correct. At the same time, the present construct contains a promoter which is activated when plants are under biotic or abiotic stress. Transformation of a plant subjected to such stress with a construct as claimed would, therefore, necessarily result in the expression of the accompanying gene. The step of expression is inherent.

REJECTION UNDER 35 USC §102(B) AND §103(A)

The examiner rejects claims 55-56, 58-63, 65-67, 69, 74, 76, 77, 82, 84-85, and 90 under §102(b) as anticipated by, and claims 55-99 under §103(a) as obvious over, Struve et al. (J.Biol.Chem. 265:14, pp. 7927-7932 (1990)). Applicants reiterate their position that Struve does not disclose a functionally equivalent promoter as such is contemplated by the present invention. Claim to such a functionally equivalent

promoter is now set forward in new claim 100. For purposes of furthering the present prosecution, however, applicants have amended claim 55, and respectively submit that the present claims are clearly neither anticipated by nor obvious over Struve et al.

CONCLUSION

In view of the foregoing amendments and remarks, applicants consider that the rejections of record have been obviated and respectfully solicit passage of the application to issue.

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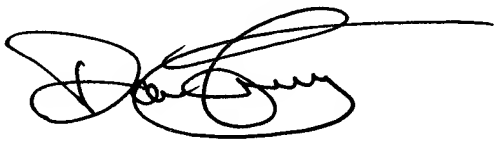
Respectfully submitted,
KEIL & WEINKAUF



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thereby enabling separations to be effected under the conditions, and with the advantages of **high-pressure liquid chromatography**.

gel fluorography the application of **fluorography** (def. 2) to the detection of substances separated in gels, as by gel electrophoresis.

gellify to cause to become a **gel** (def. 1); to become gel-like; to **gel** (def. 2).

gelonin *or* **ribosome-inactivating protein** *or* **rRNA** *N*-**glycosidase** EC 3.2.2.22; *recommended name*: rRNA *N*-glycosidase; an extremely stable, potent toxin extracted from seeds of *Gelonium multiflorum* (a plant of the spurge family). It is a single-chain glycoprotein of 28–30 kDa containing terminal mannose residues. It acts as a powerful inhibitor of protein synthesis in cell-free systems but not in intact cells; it inactivates the 60S ribosomal subunit but has no effect on the 40S subunit. Its action is to hydrolyse one specific N-glycosidic bond of an adenosine on the 28S rRNA. In cell-free protein-synthesizing systems gelonin acts like the A chains of **abrin**, **ricin**, and **modeccin**, suggesting that it lacks the ability to bind to cell surfaces and enter cells. Example from *G. multiflorum*: RIPG_GELMU, 316 amino acids (35.42 kDa).

gel-permeation chromatography a method for the separation of substances in solution, *commonly known as* **gel filtration** *or* **gel-filtration chromatography**. The separation is based mainly on exclusion effects, such as differences in molecular size and/or shape or in charge, when the stationary phase is a swollen gel. The gel used is commonly a water-swollen insoluble carbohydrate polymer from which macromolecules are excluded and migrate without retention in the interstitial fluid. Substances of low or intermediate relative molecular mass penetrate into the gel particles to an extent that is, in most instances, determined by their molecular dimensions and the degree of cross-linking of the gel. The larger molecules therefore pass through the bed more rapidly than smaller molecules. The technique can be used to determine the relative molecular mass (M_r) of unknown materials, since, for a particular column, elution occurs at a volume determined by the equation

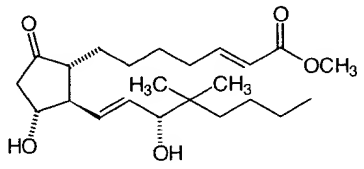
$$V_R/V_0 = 1 - \rho\log(M_r/M_{r0})$$

where V_R is the elution volume of the unknown, V_0 is the volume of the mobile phase in the column, M_r is the M_r of the unknown, M_{r0} is the M_r of the largest totally permeating molecule, and ρ is a factor that is a property of the column. Thus each column must be calibrated using standard proteins, and a plot made of the elution volumes against $\log M_r$ of the standards, from which the unknown M_r can be determined.

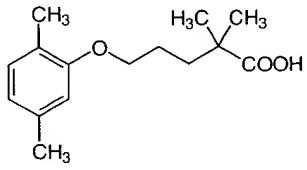
gelsolin a heat-labile, monomeric protein of apparent M_r 90 000 isolated from macrophages, platelets, and plasma. It appears to promote the gel–sol transformation of **actin** and may thereby be important in the control of locomotion, secretion, and endocytosis in these and other cells; β-actin has a similar action. There are two forms of gelsolin, plasma and cytoplasmic, generated by alternative splicing. The cytoplasmic, calcium-regulated, actin-modulating form binds to the barbed ends of actin monomers or filaments, preventing monomer exchange; it also promotes nucleation and binds with high affinity to fibronectin. Example (cytoplasmic form) from mouse: database code GELS_MOUSE, 731 amino acids (80.79 kDa).

gem- *prefix (in chemical nomenclature)* denoting the presence of **geminal** substituents.

gemeprost 16,16-dimethyl-*trans*-Δ^2-prostaglandin E_1 methyl ester; 11,15-dihydroxy-16,16-dimethyl-9-oxoprosta-2,13-dien-1-oic acid methyl ester; an analogue of **prostaglandin** E_1 with uterine stimulant activity.



gemfibrozil 2,2-dimethyl-5-(2,5-xylyloxy)valeric acid; an antihyperlipoproteinemic agent with actions similar to **clofibrate.**



geminal *(in chemistry)* describing two like groups or atoms attached to the same atom in a molecule, i.e. the geminal groups or atoms are separated by two bonds attached to the same atom. The presence of geminal substituents is denoted by the prefix *gem-* attached to the name of the compound. *Compare* **vicinal** (def. 2).

geminate occurring in pairs; doubled, twin.

+gen *or (after a consonant)* **+ogen** *comb. form* signifying producing or capable of producing (either directly or indirectly). In biological sciences it is used especially (1) with word-stems relating to physiological or pathological processes, states, conditions, etc., to denote a causative agent (e.g. antigen, lactogen, mutagen, estrogen); (2) with names of certain proteinases or blood components, to denote their inactive precursors or substances from which they can be derived by enzymic action (e.g. angiotensinogen, caseinogen, fibrinogen, trypsinogen) (*see also* **pro+** (def. 3), **zymogen**); (3) with names or name-roots of certain metabolites, to denote either a storage substance (e.g. glycogen, phosphagen) or a biosynthetic precursor (e.g. porphobilinogen); (4) with word-stems relating to physical properties (e.g. chromogen, luminogen). —**+genic** *or* **+genous** *adj. suffix.*

Genaminox KC *the proprietary name for* detergents similar to lauryldimethylamine oxide, but with different alkyl chain lengths (9–13).

Genapol *the proprietary name for* a series of nonionic polyoxyethylene detergents of the general formula $CH_3(CH_2)_x$–$O(CH_2CH_2O)_y$–H; Genapol X-080 has x = 12, y = 8, CMC 0.06–0.15 mM; Genapol X-100 has x = 12, y = 10, aggregation number 88, CMC 0.15 mM. *Compare* **C_xE_y**, **Lubrol**, **Triton**, **Tween**.

GenBank a large database of protein and nucleic-acid sequences. *See* **Appendix E**.

gene in classical genetics, a statistical entity that correlates with a particular phenotypic characteristic; the functional unit of heredity. Before their biochemical nature was understood, genes were defined in terms of units of mutation and/or recombination. Discovery of the role of DNA in genetic processes, followed by elaboration of the **central dogma** of protein synthesis, led to enunciation of the 'one gene–one enzyme' hypothesis, i.e. that a gene consisted of DNA that coded for a protein that performed the functions associated with the phenotypic expression of the gene. In current molecular genetics, the concept requires modification in a number of ways. First, the genomic DNA that codes for a polypeptide is associated with regulatory sequences such as promoters. Second, the polypeptide resulting from translation of mRNA may be subsequently split to give several polypeptides with different functions (*see* **polyprotein**). Third, the RNA transcribed may give rise to several different proteins as a result of **alternative splicing**. Three types of genes are now distinguished: those that are both transcribed into mRNA and translated into polypeptides (**structural genes**); those that are only transcribed into RNA (e.g. rRNA, tRNA); and those that function as regulators of the expression of the other two types (**regulator genes**). In diploid organisms a gene may occur in alternative forms

(alleles). The term gene is sometimes used interchangeably with **cistron**.

gene amplification the selective, repeated replication of a certain gene or genes without a proportional increase in other genes in the genome. It occurs, e.g., in the DNA puffs of *Rhynchosciara* and some other flies and in the amplification of the genes coding for ribosomal RNA (so-called ribosomal DNA) in amphibian oocytes.

gene bank *an alternative name for* **gene library**.

gene cloning *see* **molecular cloning**.

gene cluster *or* **gene complex** any group of two or more functionally related genes that are closely linked on a chromosome. The genes of a gene cluster are often structural genes coding for the enzymes that catalyse the various steps of a metabolic pathway.

gene complex *an alternative name for* **gene cluster**.

gene dosage the number of times a particular gene is present in the genome.

gene duplication the phenomenon, occurring in some higher organisms, in which there is duplication of the DNA sequences representing particular genes. This process is thought to have played a decisive part in the evolution of these organisms, through the occurrence of different mutations in the two duplicated genes.

gene expression the process by which the information carried by a gene or genes becomes manifest as the phenotype. It involves **transcription** of the gene into complementary RNA sequences and, for structural genes, subsequent **translation** of mRNA into polypeptide chains and their assembly into the ultimate protein products. Gene expression is tightly regulated by **promoters, enhancers**, and **transcription factors**.

gene frequency a measure of the proportion of an allele in a given population, equal to the number of loci at which a given allele occurs, divided by the total number of loci at which it could occur.

gene library *or* **cloned library** *or* **gene bank** *or* **shotgun collection** a random collection of DNA fragments cloned in a **vector** (def. 3), and which may include all the genetic information of a particular species. It may be prepared from a variety of sources, including an extract of mRNA, in contrast to a **genomic library** which is prepared from genomic DNA.

gene mutation any **mutation** (def. 1) occurring within a single gene.

gene pool the sum of the genetic information in the reproductive members of a population of sexually reproducing organisms.

gene product any of the types of RNA (transcription products) or any of the proteins or protein subunits (translation products) synthesized biochemically on the basis of the information encoded in a genome.

general acid-catalysis **homogeneous catalysis** in which the catalysts are various hydron donors (acids). *Compare* **specific acid-catalysis**.

general base-catalysis **homogeneous catalysis** in which the catalysts are various hydron acceptors (bases). *Compare* **specific base-catalysis**.

generally labelled describing the labelling of a molecule in such a way that a radionuclide may be present at any or all (but not necessarily all) possible positions. *Compare* **uniformly labelled**.

general transcription factor any of the proteins whose assembly around the **TATA box** is required for the initiation of transcription of most eukaryotic genes.

generate *(in mathematics)* to conceive a point, line, or surface to be moving in a specified way so as to form a line, surface, or solid, respectively.

generation **1** the act or process of producing or reproducing, naturally or artificially. **2** the phase in a life cycle that extends from one to the immediately successive reproduction. **3** any group comprising all those members of a population who are equally removed from a common ancestor or from coeval ancestors.

generation of diversity *(in immunology)* the process by which a large number of variable regions are generated in the immunoglobulins. The **stem cell** genome contains multiple variants of L-chain V (variable) and J genes and of the H-chain V, J, and D (diversity) genes. As the stem cells differentiate, the maturing lymphocyte constructs particular L and H genes of virtually unique structure by a recombination process that randomly selects one out of each set of gene segments and assembles them, together with a C (for the constant region) gene into a mature H or L gene. This, combined with recombinational inaccuracies, somatic point mutations, and the varied combinations of L and H chains found in immunoglobulins results in a repertoire of millions of lymphocytes each with H and L genes encoding unique molecules. *See also* **immunoglobulin**.

generation time the time between division of a cell and that of its daughter cells, averaged over a whole cell population.

gene redundancy the presence in a cell of many copies of a single gene. The multiple copies may be inherited or result from selective **gene duplication** during development.

gene-regulatory protein any protein that binds to a specific DNA sequence to alter the expression of a gene.

+genesis *comb. form* denoting beginning or origin; development; generation. *See also* **+gen**. —**+genetic** *or* **+genic** *adj. comb. form.*

gene splicing biochemical and/or chemical manipulations with the object of attaching one DNA molecule to another. The neatest method is to cleave the DNA to be inserted (foreign DNA) with a **restriction endonuclease** that yields single-stranded ends that are complementary to each other. The **cloning vector** into which the foreign DNA is to be inserted is treated with the same endonuclease so that the complementary ends of the two DNAs specifically associate under annealing conditions and are subsequently covalently joined (spliced) through the action of **DNA ligase**. If the endonuclease produces fragments with 'blunt' or **flush ends** then a similar procedure is adopted. If the foreign DNA and the cloning vector have no common restriction sites then terminal **deoxynucleotidyl transferase** may be used which adds nucleotides to the 3′-terminal OH group of a DNA chain. For this purpose tails of poly(dT) and poly(dA) may be used. The transformed cells are then grown and those containing the spliced DNA are selected (cloning). The preferred method of splicing is one that allows the foreign DNA to be removed easily by means of a restriction endonuclease, preferably the same one that was initially used in splicing. By this means large amounts of the foreign DNA can be synthesized and used for many different purposes. Alternatively the cloned cells containing the foreign DNA can be used to permit the expression of a foreign protein which is then recovered.

genetic *or* **genetical** of or pertaining to **genetics**, **genes**, or the origin of something. —**genetically** *adv.*

genetically engineered describing a cell, strain, or organism whose phenotype has been altered by manipulation of its genetic material. *See* **genetic engineering**.

genetic block a reduction in the activity of a particular enzyme in a metabolic pathway as a result of gene mutation. A genetic block is termed **complete** when the particular enzyme activity is absent, or **incomplete** (*or* leaky) when the enzyme formed is defective and of limited activity.

genetic carrier *see* **carrier** (def. 9).

genetic code all the regularities in nucleotide sequence according to which genetic information for the sequences of all the polypeptides synthesized by transcription and translation is encoded in DNA (or RNA in some viruses). A sequence of three nucleotide residues (a codon) is required to code for one amino-acid residue, and since there are four different kinds of base in nucleic acids (apart from minor constituents), 4^3 i.e. 64 different nucleotide triplets can exist. But only 20 different amino-acid residues in polypeptides can be coded for; therefore the code is degenerate in that most amino acids can be